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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

CHOO et al.

Serial No.: Unassigned (National filing of PCT/GB00/02080)

Filing Date: herewith

Art Unit: Unassigned

Examiner: Unassigned

Title: MOLECULAR SWITCHES

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

This Preliminary Amendment accompanies the filing for a National Phase application of PCT/GB00/02080. Entry of the following amendments is respectfully requested.

I. AMENDMENTS

In the specification:

On page 1, line 3, before "Field of the Invention," please insert the following paragraph:

-- Cross Reference to Related Applications

This applications claims priority under 35 U.S.C. §365(c) and 35 U.S.C. §120 to PCT/GB00/02080 and priority under 35 U.S.C. §119/363 to United Kingdom applications serial nos. 9912635.1 and 0001582.6.--

In the claims:

Before claim 1, please insert the following paragraph:

-- What is claimed is:--

Please amend the claims as follows:

3. (Amended) A method according to claim 1, in which one of the first molecule and second molecule comprises a nucleic acid binding molecule, and the other of the first and second molecules comprises a nucleic acid.

4. (Amended) A method according to Claim 1, in which one or both of the candidate nucleic acid and nucleic acid binding molecules is provided as a plurality of molecules.

6. (Amended) A method according to Claim 4, in which a single target nucleic acid is used.

7. (Amended) A method according to Claim 4, in which one of the components isolated and/or identified in step (c) is a ligand component.

8. (Amended) A method according to claim 4, in which one of the components isolated in step (c) is a nucleic acid binding molecule component.

9. (Amended) A method according to claim 4, in which the nucleic acid is provided as a library of nucleic acid sequences, the sequences being related to one another by sequence homology.

10. (Amended) A method according to claim 4, in which a plurality of candidate ligands are used.

11. (Amended) A method according to claim 4, in which the ligands are provided as a library of ligands.

12. (Amended) A method according to claim 4, in which the candidate nucleic acid binding molecules are polypeptides.

13. (Amended) A method according to claim 4, in which the polypeptides are at least partly derived from DNA binding proteins, preferably transcription factors.

14. (Amended) A method according to claim 4, in which the candidate nucleic acid binding molecules are derived from zinc finger transcription factors.

15. (Amended) A method according to claim 4, in which the candidate nucleic acid binding molecules are provided as a phage display library.

16. (Amended) A method according to claim 4, in which the ligand is selected from Distamycin A, Actinomycin D and echinomycin.

17. (Amended) A switching system comprising a gene switch, in which the switching system has been selected by a method according to claim 4.

18. (Amended) A method of regulating transcription from a nucleic acid sequence comprising providing a target nucleic acid to which a nucleic acid binding molecule selected according to the method of claim 4 binds in a manner modulatable by a ligand and binding the nucleic acid binding molecule to the target nucleic acid such that transcription is regulated..

Please cancel claims 19 and 20 without prejudice or disclaimer.

21. (Amended) A method of modulating the expression of one or more genes, said method comprising administering a nucleic acid binding molecule and a ligand selected according to the method of claim 4 to a cell, in which the regulatory sequences of the genes comprise a target nucleic acid selected according to the method of claim 4.

23. (Amended) A method according to Claim 21 wherein the host cell is a plant cell.

27. (Amended) A method according to Claim 1, in which each of the first and second molecules comprises a polypeptide.

29. (Amended) A method according to Claim 27, in which one or both of the first and second molecules is provided as a library of polypeptides.

30. (Amended) A method according to Claim 27, in which the ligands are provided as a library of ligands.

31. (Amended) A method according to claim 27, in which the ligand is an immunoglobulin molecule, preferably an antibody molecule.

32. (Amended) A method according to claim 27, in which the first molecule is a nucleic acid binding protein capable of binding to nucleic acid.

34. (Amended) A switching system comprising a protein switch, in which the switching system has been selected by the method of claim 27.

35. (Amended) A method of regulating transcription from a nucleic acid sequence comprising providing a target nucleic acid to which a nucleic acid binding protein selected by the method according to claim 33 binds and binding the nucleic acid binding protein to the target nucleic acid, thereby regulating transcription.

Please cancel claims 36 and 37, without prejudice or disclaimer.

41. (Amended) A method according to Claim 39 wherein the host cell is a plant cell.

42. (Amended) A method according to Claim 41, in which the plant cell is part of a plant and the target sequence is part of a regulatory sequence to which the nucleotide sequence of interest is operably linked, said regulatory sequence being preferentially active in the male or female organs of the plant.

44. (Amended) An organism according to Claim 43, in which any or all of the first nucleic acid sequence, the second nucleic acid sequence, and the target nucleic acid sequence are heterologous to the organism.

45. (Amended) A transgenic non-human organism according to Claim 43 which is a plant.

46. (Amended) A method according to claim 1, in which the first molecule component of the complex has a higher affinity for the second molecule component of the complex in the presence of the ligand component than in the absence of the ligand component.

47. (Amended) A method according to claim 1, in which the first molecule component of the complex has a higher affinity for the second molecule component of the complex in the absence of the ligand component than in the presence of the ligand component.

Attached hereto is a version showing changes made to the claims and the currently pending claim set.

II. REMARKS

The specification has been amended to include the cross reference to related applications. The claims have been amended to eliminate improper multiple dependencies prior to examination. No new matter has been added as a result of these amendments and entry thereof is respectfully requested. Applicants reserve the right to pursue the subject matter of the original, multiple dependent claims in this or related applications.

Respectfully submitted,

Date: Nov 28, 2001

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Version with Markings to Show Changes Made

In the specification:

On page 1, line 3, before "Field of the Invention," the following paragraph has been inserted:

Cross Reference to Related Applications

This applications claims priority under 35 U.S.C. §365(c) and 35 U.S.C. §120 to PCT/GB00/02080 and priority under 35 U.S.C. §119/363 to United Kingdom applications serial nos. 9912635.1 and 0001582.6.

In the claims:

Before claim 1, the following paragraph has been inserted:

What is claimed is:

The claims have been amended as follows:

3. (Amended) A method according to claim 1 [Claim 1 or Claim 2], in which one of the first molecule and second molecule comprises a nucleic acid binding molecule, and the other of the first and second molecules comprises a nucleic acid.

4. (Amended) A method according to Claim 1[, 2 or 3,] in which one or both of the candidate nucleic acid and nucleic acid binding molecules is provided as a plurality of molecules.

6. (Amended) A method according to Claim 4 [or 5], in which a single target nucleic acid is used.

7. (Amended) A method according to Claim 4, [5 or 6,] in which one of the components isolated and/or identified in step (c) is a ligand component.

8. (Amended) A method according to [any of Claims 4 to 7] claim 4, in which one of the components isolated in step (c) is a nucleic acid binding molecule component.

9. (Amended) A method according to [any of Claims 4 to 8] claim 4, in which the nucleic acid is provided as a library of nucleic acid sequences, the sequences being related to one another by sequence homology.

10. (Amended) A method according to [any of Claims 4 to 9] claim 4, in which a plurality of candidate ligands are used.

11. (Amended) A method according to [any of Claims 4 to 10] claim 4, in which the ligands are provided as a library of ligands.

12. (Amended) A method according to [any of Claims 4 to 11] claim 4, in which the candidate nucleic acid binding molecules are polypeptides.

13. (Amended) A method according to [any of Claims 4 to 12] claim 4, in which the polypeptides are at least partly derived from DNA binding proteins, preferably transcription factors.

14. (Amended) A method according to [any of Claims 4 to 12] claim 4, in which the candidate nucleic acid binding molecules are derived from zinc finger transcription factors.

15. (Amended) A method according to [any of Claims 4 to 13] claim 4, in which the candidate nucleic acid binding molecules are provided as a phage display library.

16. (Amended) A method according to [any of Claims 4 to 14] claim 4, in which the ligand is selected from Distamycin A, Actinomycin D and echinomycin.

17. (Amended) A switching system comprising a gene switch, in which the switching system has been selected by a method according to [any of Claims 4 to 15] claim 4.

18. (Amended) [Use of a nucleic acid binding molecule selected by a method according to any one of Claims 4 to 15 in a] A method of regulating transcription from a nucleic acid sequence comprising providing a target nucleic acid to which [the] a nucleic acid binding molecule selected according to the method of claim 4 binds in a manner modulatable by a ligand and binding the nucleic acid binding molecule to the target nucleic acid such that transcription is regulated..

19 and 20. Canceled.

21. (Amended) A method of modulating the expression of one or more genes, said method comprising administering a nucleic acid binding molecule and a ligand selected according to the method of [any one of Claims 4 to 15] claim 4 to a cell, in which the regulatory sequences of the genes comprise a target nucleic acid selected according to [a] the method [according to any of Claims 4 to 15] of claim 4.

23. (Amended) A method according to Claim 21 [or 22] wherein the host cell is a plant cell.

27. (Amended) A method according to Claim 1 [or 2], in which each of the first and second molecules comprises a polypeptide.

29. (Amended) A method according to Claim 27 [or 28], in which one or both of the first and second molecules is provided as a library of polypeptides.

30. (Amended) A method according to Claim 27[, 28 or 29], in which the ligands are provided as a library of ligands.

31. (Amended) A method according to [any of Claims 27 to 30] claim 27, in which the ligand is an immunoglobulin molecule, preferably an antibody molecule.

32. (Amended) A method according to [any of Claims 27 to 31] claim 27, in which the first molecule is a nucleic acid binding protein capable of binding to nucleic acid.

34. (Amended) A switching system comprising a protein switch, in which the switching system has been selected by [a] the method [according to any of Claims 27 to 33] of claim 27.

35. (Amended) [Use of a nucleic acid binding protein selected by a method according to Claim 33, in a] A method of regulating transcription from a nucleic acid sequence comprising providing a target nucleic acid to which [the] a nucleic acid binding protein selected by the method according to claim 33 binds and binding the nucleic acid binding protein to the target nucleic acid, thereby regulating transcription.

36 and 37. Canceled.

41. (Amended) A method according to Claim 39 [or 40] wherein the host cell is a plant cell.

42. (Amended) A method according to Claim [42] 41, in which the plant cell is part of a plant and the target sequence is part of a regulatory sequence to which the nucleotide sequence of interest is operably linked, said regulatory sequence being preferentially active in the male or female organs of the plant.

44. (Amended) An organism [A method] according to Claim 43, in which any or all of the first nucleic acid sequence, the second nucleic acid sequence, and the target nucleic acid sequence are heterologous to the organism.

45. (Amended) A transgenic non-human organism according to Claim 43 [or 44] which is a plant.

46. (Amended) A method according to [any of Claims 1 to 16 and 27 to 33] claim 1, in which the first molecule component of the complex has a higher affinity for the second molecule component of the complex in the presence of the ligand component than in the absence of the ligand component.

47. (Amended) A method according to [of Claims 1 to 16 and 27 to 33] claim 1, in which the first molecule component of the complex has a higher affinity for the second molecule component of the complex in the absence of the ligand component than in the presence of the ligand component.

Currently Pending Claim Set

1. A method of selecting a switching system, the switching system comprising: (i) a first component comprising a first molecule and (ii) a second component comprising a second molecule, in which the first molecule binds to the second molecule in a manner modulatable by a ligand, and (iii) a third component comprising the ligand, the method comprising the steps of:

(a) contacting one or more candidate first molecules with one or more candidate second molecules in the presence of one or more ligands;

(b) selecting a complex of the three components;

(c) optionally isolating and/or identifying the unknown components of the complex;

(d) comparing the binding of the first molecule component of the complex to the second molecule component of the complex in the presence and absence of the ligand component of the complex; and

(e) selecting complexes where said binding differs in the presence and absence of the ligand component,

in which at least one component is provided in the form of a library of members.

2. A method according to Claim 1, in which at least one of the candidate first molecules comprises a non-naturally occurring binding domain which binds to the second molecule.

3. (Amended) A method according to claim 1, in which one of the first molecule and second molecule comprises a nucleic acid binding molecule, and the other of the first and second molecules comprises a nucleic acid.

4. (Amended) A method according to Claim 1, in which one or both of the candidate nucleic acid and nucleic acid binding molecules is provided as a plurality of molecules.

5. A method according to Claim 4, in which the nucleic acid binding molecule is provided as a library of nucleic acid binding molecules.

6. (Amended) A method according to Claim 4, in which a single target nucleic acid is used.

7. (Amended) A method according to Claim 4, in which one of the components isolated and/or identified in step (c) is a ligand component.

8. (Amended) A method according to claim 4, in which one of the components isolated in step (c) is a nucleic acid binding molecule component.

9. (Amended) A method according to claim 4, in which the nucleic acid is provided as a library of nucleic acid sequences, the sequences being related to one another by sequence homology.

10. (Amended) A method according to claim 4, in which a plurality of candidate ligands are used.

11. (Amended) A method according to claim 4, in which the ligands are provided as a library of ligands.

12. (Amended) A method according to claim 4, in which the candidate nucleic acid binding molecules are polypeptides.

13. (Amended) A method according to claim 4, in which the polypeptides are at least partly derived from DNA binding proteins, preferably transcription factors.

14. (Amended) A method according to claim 4, in which the candidate nucleic acid binding molecules are derived from zinc finger transcription factors.

15. (Amended) A method according to claim 4, in which the candidate nucleic acid binding molecules are provided as a phage display library.

16. (Amended) A method according to claim 4, in which the ligand is selected from Distamycin A, Actinomycin D and echinomycin.

17. (Amended) A switching system comprising a gene switch, in which the switching system has been selected by a method according to claim 4.

18. (Amended) A method of regulating transcription from a nucleic acid sequence comprising providing a target nucleic acid to which a nucleic acid binding molecule selected according to the method of claim 4 binds in a manner modulatable by a ligand and binding the nucleic acid binding molecule to the target nucleic acid such that transcription is regulated..

19 and 20. Canceled.

21. (Amended) A method of modulating the expression of one or more genes, said method comprising administering a nucleic acid binding molecule and a ligand selected according to the method of claim 4 to a cell, in which the regulatory sequences of the genes comprise a target nucleic acid selected according to the method of claim 4.

22. A method of modulating the expression of one or more nucleotide sequences of interest in a host cell which host cell comprises a nucleic acid sequence capable of directing the expression of a nucleic acid binding molecule and a target nucleic acid sequence to which the nucleic acid binding molecule binds in a manner modulatable by a ligand, which method comprises administering said ligand to the cell and wherein the nucleic acid binding molecule is heterologous to the host cell.

23. (Amended) A method according to Claim 21 wherein the host cell is a plant cell.

24. A method according to Claim 23, in which the plant cell is part of a plant and the target sequence is part of a regulatory sequence to which the nucleotide sequence of interest is operably linked, said regulatory sequence being preferentially active in the male or female organs of the plant.

25. A non human transgenic organism comprising a target nucleic acid sequence and a nucleic acid sequence capable of directing the expression of a nucleic acid binding molecule which binds to the target nucleic acid in a manner modulatable by a ligand, in which the target nucleic acid sequence and/or nucleic acid sequence are heterologous to the organism.

26. A transgenic non-human organism according to Claim 25 which is a plant.

27. (Amended) A method according to Claim 1, in which each of the first and second molecules comprises a polypeptide.

28. A method according to Claim 27, in which the first molecule comprises a polypeptide binding protein and the second molecule comprises a polypeptide.

29. (Amended) A method according to Claim 27, in which one or both of the first and second molecules is provided as a library of polypeptides.

30. (Amended) A method according to Claim 27, in which the ligands are provided as a library of ligands.

31. (Amended) A method according to claim 27, in which the ligand is an immunoglobulin molecule, preferably an antibody molecule.

32. (Amended) A method according to claim 27, in which the first molecule is a nucleic acid binding protein capable of binding to nucleic acid.

33. A method according to Claim 32, in which the nucleic acid binding protein binds to nucleic acid in a manner modulatable by the second molecule.

34. (Amended) A switching system comprising a protein switch, in which the switching system has been selected by the method of claim 27.

35. (Amended) A method of regulating transcription from a nucleic acid sequence comprising providing a target nucleic acid to which a nucleic acid binding protein selected by the method according to claim 33 binds and binding the nucleic acid binding protein to the target nucleic acid, thereby regulating transcription.

36 and 37. Canceled.

38. A method of modulating the expression of one or more genes, said method comprising administering a nucleic acid binding protein and a ligand selected according

to a method according to Claim 33 to a cell, in which the regulatory sequences of the genes comprise a target nucleic acid to which the nucleic acid binding protein binds in a manner modulatable by a ligand.

39. A method of modulating the expression of one or more nucleotide sequences of interest in a host cell which host cell comprises a first nucleic acid sequence capable of directing the expression of a nucleic acid binding protein, a second nucleic acid sequence capable of directing the expression of a second polypeptide, the binding between the nucleic acid binding to the second polypeptide being modulatable by a ligand, and a target nucleic acid sequence to which the nucleic acid binding protein binds in a manner modulatable by a second polypeptide,which method comprises administering said ligand to the cell.

40. A method according to Claim 39, in which the nucleic acid binding protein is heterologous to the host cell.

41. (Amended) A method according to Claim 39 wherein the host cell is a plant cell.

42. (Amended) A method according to Claim 41, in which the plant cell is part of a plant and the target sequence is part of a regulatory sequence to which the nucleotide sequence of interest is operably linked, said regulatory sequence being preferentially active in the male or female organs of the plant.

43. A non human transgenic organism comprising a target nucleic acid sequence, a first nucleic acid sequence capable of directing the expression of a nucleic acid binding protein, and a second nucleic acid sequence capable of directing the expression of a second polypeptide which binds to the nucleic acid binding protein in a manner

modulatable by a ligand, in which the nucleic acid binding protein binds to the target nucleic acid sequence in a manner modulatable by binding of the second polypeptide.

44. (Amended) An organism according to Claim 43, in which any or all of the first nucleic acid sequence, the second nucleic acid sequence, and the target nucleic acid sequence are heterologous to the organism.

45. (Amended) A transgenic non-human organism according to Claim 43 which is a plant.

46. (Amended) A method according to claim 1, in which the first molecule component of the complex has a higher affinity for the second molecule component of the complex in the presence of the ligand component than in the absence of the ligand component.

47. (Amended) A method according to claim 1, in which the first molecule component of the complex has a higher affinity for the second molecule component of the complex in the absence of the ligand component than in the presence of the ligand component.